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"Method and system for quality management in therapeutic processes"

DESCRIPTION

The present invention relates to a process for quality management in therapeutic processes. It also relates to a system for its implementation.

The new therapeutic protocols involved at the level of cells and genes require a high level of reliability and security owing to the complexity of the operations carried out, the number of stages and personnel involved in the protocol. The quality requirement is even more crucial as these new therapies relate to the elementary blocks of human beings and are moreover the subject of justified vigilicance on the part of health authorities. It is moreover essential to guarantee total tracability of samples.

Cell therapy kits, for example the MAK™ kit produced by the company IDM, are currently finalized for supply to the laboratories in charge of treating cell samples taken from patients for whom clinicians have prescribed this therapeutic protocol. The cells treated in this way are reinjected into these patients.

In these therapeutic processes, both biological elements and physical objects are treated: the sample bags each associated with a patient and information: data associated with these bags and which indicate, in particular, the operators and the process state of progress.

The stages of treatment of the bags of cells are subjected to Standard Operating Procedures (SOPs) which are fully codified. Observance of these procedures ensures the quality of treatment required in order to be approved. However, the complexity of these procedures, the participation of several entities which are partners in the treatment processes, the need to rationalize the management of the increasingly automated therapeutic processes and the wish for vigilance expressed by the health authorities have led to the observation that it is not possible to segment responsibility for the management of therapeutic process

quality while counting only on each individual participant in the therapeutic process.

The document US 5 307 262 describes a process and system for quality management of clinical data related to patients. The process is implemented in the form of a computer program controlled by menus and in particular envisages data input concerning a patient, the entry of a command launching the quality control of this data, the displaying on screen of possible messages resulting from these controls, and if the operator judges this to be necessary, the provision and printing of one or more worksheets including messages that the operator chose from a menu, intended to facilitate the correction of data by the person or persons concerned (for example a specialist).

The document WO 94 27238 describes a testing system for microbiological specimens, including at least one workstation linked/connected to a database containing information relating to patients and a microbiological database. In particular, this system envisages the attribution of an identification number allowing access to the database and to link each tested specimen with the information relating to the patient concerned, the input of data relative to the test performed on the specimen using screen pages and the provision of a report.

The document US 5 072 303 describes a processing system for instructions and prescriptions within a hospital environment, including in particular the automatic updating of a task list in response to instructions or orders issued by the hospital doctors or nurses.

The purpose of the invention is to propose a quality management process which guarantees total consistency in the search for security and tracability throughout the different stages of the therapeutic process.

This objective is achieved with a process for the management of quality in a therapeutic process, this therapeutic process comprising the stages of taking cells from a patient, a specific treatment of these cells using a

specific treatment protocol, and reinjection into the patient of said cells treated in this way.

According to the invention, the process comprises:

- stages of identification of the entities involved in the therapeutic process,

- stages of sequential and conditional validation of the stages of the therapeutic process, and

- stages of quality control in which data acquired during said validation stages are processed in order to supply information on the quality of the realization of said therapeutic process, said stages of identification, validation and control being carried out for each batch of samples taken from a given patient.

In this way, with the process according to the invention, it becomes possible to provide checking and follow-up of complex therapeutic processes involving several entities and requiring total tracability.

A major advantage of the quality management process according to the invention in fact resides in the fact that it is based on the idea that a batch is associated with each patient, and that this batch and its associated data must be followed throughout the process. In particular, the standard operating procedures (SOP) can be followed and validated, ensuring a high level of tracability, reliability, and security.

When the quality management process according to the invention is implemented in a therapeutic process involving

several entities, optionally remote, and is associated with a standard operating procedure for preparation comprising a series of functional stages, this process then preferably comprises:

- stages of validation respectively associated with each of the functional stages, the passing from one validation stage to the following validation stage being conditional on the results of the processing of data collected during this validation stage, and
- a stage of processing of the information and data collected in the different validation stages, in order to issue final certification of a preparation carried out according to the standard operating procedure and/or a list of the anomalies detected during the preparation.

In a preferred implementation of the invention, validation of the final certification is conditional on the input of a validation password.

The quality management process according to the invention is advantageously implemented in the form of software installed on a data processing system. With each validation stage is associated at least one screen page which can be accessed on the display means of at least one workstation connected to the data processing system.

Each screen page comprises a coded identification field for a patient which matches the batch of samples subjected to the standard operating procedure.

It can advantageously be envisaged for the exit from certain stages of the process to be conditional on printing the screen pages corresponding to these stages.

In the case of a quality management process implemented in a preparation laboratory receiving therapeutic kits from at least one operational entity, this process then further comprises stages for monitoring the transfer of these kits.

When the preparation laboratory deals with a cytapheresis service, the quality management process further comprises stages for monitoring the receipt of cytapheresis pouches.

According to another aspect of the invention, a quality management system is proposed for the implementation of the process according to the invention. The functions of this quality management system can further be extended to include the management of other sectors of the preparation laboratory involved in the therapeutic process. Moreover, this system is preferably connected to a communications network, open or closed, for exchanging data with other entities involved in a therapeutic process.

The invention relates to a quality management system allowing the setup of other similar therapeutic protocol preparation processes and then their control and management within the same system.

Further features and advantages of the invention will appear in the description below. In the attached drawings, given as non-limitative examples:

- Figure 1 shows a quality management system according to the invention organized around one operator;
- Figure 2 shows a quality management organization involving several therapeutic processes;
- Figure 3 shows the different stages of a therapeutic process with which a quality management process according to the invention is associated;
- Figure 4 shows the essential stages of the software implementing the quality management process according to the invention;
- Figure 5 is a schematic representation of a screen page providing access to all the quality management stages;
- Figure 6 is a schematic representation of a screen page corresponding to a stage of preparation of an autologous serum;
- Figure 7 is a schematic representation of a screen page corresponding to a stage of bacteriological control;
- Figure 8 is a schematic representation of a screen page corresponding to a stage of quality control test result input;
- Figure 9 is a schematic representation of a screen

page corresponding to a stage of retrospective analysis;

- Figure 10 is a schematic representation of a screen page corresponding to a stage of final certification;

- Figure 11 is a schematic representation of a screen page corresponding to a stage of listing anomalies; and

- Figure 12 is a schematic representation of a screen page corresponding to a stage of transfer from the preparation laboratory to the treatment centre.

There follows a description of an example of implementation of the process according to the invention, in the area of cell therapy.

The parties involved in the operation of the process according to the invention are, with reference to Figure 1:

- an entity EX controlling operation of the process according to the invention and distributing the therapeutic kits KT,

- treatment centres CT, CTi, CTn run by clinicians CL, CLi, CLn who, for their patients PA, PAi, PAn, take the initiative of starting therapeutic protocols,

- preparation laboratories L1, Li, Ln which prepare, analyze and pack the products used in these therapeutic protocols,

- cytapheresis services CY, CYi, CYn which take samples from patients and make reinjections into them,

- bacteriological testing laboratories CB, CBi, CBn, and optionally collection centres CR separate from the operational entity EX.

The main stages of the therapeutic process controlled by the quality management process according to the invention are specified in several examples schematically illustrated in Figure 1.

In a first configuration encountered in the operation of the process according to the invention and described sequentially in Figure 3,

- 1/ a clinician CL in charge (0) of a patient PA within a treatment centre CT, issues a diagnosis DI and decides to contact a preparation laboratory L1 in order to start one or

more protocols intended for his patient,

- 2/ this laboratory L1 then contacts the operational entity EX for the therapeutic protocol process for it to supply it with the therapeutic kits corresponding to this protocol,

- 3/ the laboratory L1 also contacts a cytapheresis service CY with a view to organizing taking a plasma sample from the patient; a sample PR is taken from the patient;

- 4/ the laboratory L1 receives the therapeutic kit KT and an associated cytapheresis sheet from the operational entity EX or from a collection centre; the standard operating procedure(s) (SOP's) is/are then initiated,

- 5/ the laboratory L1 receives sample pouches from the cytapheresis service CY;

- 6/ the contents of these pouches are treated (TR) by the laboratory according to a standard operating procedure SOP and under the control of the quality management process according to the invention,

- 7/ then, when a final certification F is granted, the treated pouches accompanied by the necessary documents are sent to the clinician who arranges reinjection RI into the patient,

- 8/ post-reinjection follow-up information is input (7') and forwarded to the operational entity EX.

The operational entity is at the heart of the therapeutic process and manages the quality control and guarantees the tracability which is essential for this type of operation. The quality management process is intimately linked to the operating procedure SOP1 implemented in the laboratory L1, but it can also be involved in the management G of this laboratory.

In another possible operating configuration of the quality management process according to the invention, part of the entities involved in the therapeutic process are integrated on a single site. In this way, the laboratory Li in charge of the preparation can for exemple include the treatment centre CTi and its clinicians CLi in charge of

patients PAi and of the cytapheresis services CYi, the bacteriological control being carried out by an external laboratory CBi. The quality management process according to the invention can then be implemented both to follow up the operating procedure SOPi and to provide quality management Gi within the other entities CYi, CTi.

It can also be envisaged for the distribution of the therapeutic kits not to be directly carried out by the operational entity Ex but assigned to a collection centre CR with which a preparation laboratory Ln is in contact for the supply of the kits. The quality management process according to the invention then handles the follow-up of the procedure SOPn and the management Gn of this preparation laboratory which is also in contact with a bacteriological control laboratory CBn, a cytapheresis laboratory and one or more treatment centres CTn to which the clinicians CLn and their patients PAn are attached. The operational entity Ex receives from each preparation laboratory the information relating to the quality management of the operating procedures and post-reinjection monitoring. This data is processed, analyzed and optionally forwarded to a supervising authority AT.

The process according to the invention can be implemented for the quality management of several therapeutic protocols, as illustrated in Figure 2.

Several therapeutic protocols can be operated by an equivalent number of operational entities EXa, EXb each controlling a network Ra, Rb of preparation laboratories $L_{a,1}$, $L_{a,2}$, $L_{a,3}$, $L_{a,i}$, $L_{a,i+1}$, $L_{a,N}$; $L_{b,1}$, $L_{b,2}$, $L_{b,3}$, $L_{b,i}$, $L_{b,i+1}$, $L_{b,i+2}$, $L_{b,M}$. These laboratories carry out preparations for the treatment centres CT of patients PA and are all equipped with software implementing the quality management process according to the invention. The operational entities EXa, EXb supply the laboratories with therapeutic kits, provide supervision of the preparation operations carried out by the laboratories, collect quality management data and report for exemple to a supervising authority AT.

The data processing tools implemented with the quality management process can furthermore provide other control and processing functions, as illustrated in the diagram in Figure 4. In this way, the quality management process according to the invention offers the operator a command bar BC which provides access in particular to the following features:

- a Guide feature, which comprises a set of information on the techniques implemented in the therapeutic process, in particular in the form of animated sequences SA, SA1, SA2,.., SAm or of video sequences;

- a full sequential follow-up of the standard operating procedures (SOPs) which constitute the heart of the software embodying the process according to the invention; this software element EL comprises in particular a set of screen pages PO, PE1,.., PEn which are consulted sequentially and filled in by the operator;

- management and archiving DB of the data collected during the operation of the quality management process;

- management LM of the preparation laboratory which can include stock management SM, personnel management PM including in particular training requirements and ongoing appraisal of this personnel,
input/output management OM, and automated management GM of the standard operating procedures;

- a network feature NM for managing communications between the laboratory L1 and the other entities involved in the therapeutic protocols, in particular with bacteriological control laboratories CB, with treatment centres CT, with cytapheresis services CY, an operational entity EX, a collection centre CR and a connection XT to other networks.

There follows a description of the main stages of the quality management process according to the invention, with reference to the corresponding screen pages encountered by operators. It is here considered that the quality management process according to the invention is implemented in the form of software installed on an I.T. workstation in a preparation laboratory.

When the process according to the invention is launched, access is controlled using known techniques in this field, for exemple a request for a password and a check on this; the password or code can be regularly validated by self-assessment tests on the user's knowledge using an interactive program.

The operator is then prompted, on a home page, to supply identification data for the different parties involved in the therapeutic process with which the control process according to the invention is associated.

As a non-limitative example, in the case of the MAK™ cell therapy protocol, the operator is asked for information on the following entities:

- the clinician,
- the laboratory in charge of the preparation of the MAK™ protocol,
- the laboratory in charge of the bacteriological control,
- the laboratory in charge of the apheresis,
- the treatment centre.

With each request for information on an entity participating in the protocol is associated a screen page the critical points of which must be completed in full by the operator before being allowed to pass to the following screen page, for security and tracability reasons. It is to be noted that each screen page contains a coded identification of a patient.

There follows a description of several exemples of screen pages designed for each of the stages of the SOP module of the quality management process according to the invention, with reference to Figures 5 to 12. Only a limited number of screen pages which are characteristic of the process are shown below.

A screen page PO (Fig. 5) provides the process operator with a table of contents E and the details RM of the laboratory in charge of the preparation, in particular the name LA of this laboratory, its postal address AD, its

telephone number TL, fax number FA and E-mail address EM as well as the name CL of the person in charge of preparations. The screen page PO also contains the preparations' start date DD and end date DF, and identification fields which are essential for the quality management process according to the invention;

- the study title ST,
- a batch number LN,
- an apheresis barcode number BC,
- a "patient" code CP.

This screen page PO, in fact like all the screen pages developed for the process according to the invention, uses a graphic interface and the different parts E1, E2, ..., Ei, ...En of the software can be selected using a mouse. The screen page can be closed using a cancellation command CA. The information can be entered using the keyboard, the mouse, vocally or by any other input means allowing the operator to work in appropriate operating conditions, in particular aseptic conditions.

After a screen page (not illustrated) corresponding to the parameters for the collection stage of a treatment kit, the quality management process operator must complete a screen page PEi corresponding to the preparation of an autologous serum. This screen page comprises, as a non-limitative example, a title EP, a reminder of the patient code CP and of the date D, and a series of operational instructions S1, S2, ..., Sj, ...Sn which must be carried out in sequence. Data entered by the operator can be associated with each of these instructions. When all of these operations have been carried out, selection of a validation key VA orders the page to be closed, which is only confirmed if all the instructions have been carried out.

Bacteriological control stages are envisaged throughout the preparation process. The screen page EB (Fig. 7) corresponds to one of these bacteriological control stages. It generally comprises a header containing a title EC, a reminder of the study ST, of the patient code CP and of the

date D, a module RM indicating the details of the laboratory responsible for the preparation and the batch number LN, and a module BS containing the data relating to the bacteriological control, in particular the address AB of the laboratory in charge of the bacteriological control, an indication OB of the control operator, the results TB of a set of bacteriological control tests and the date DB of these tests. This screen page EB further comprises an indication AL that printing of this screen page is mandatory. A print command icon PR is provided for this purpose.

When all the stages of the standard operating procedure SOP have been executed, a screen page ER lists all the results of the quality tests which must be entered by the operator. This screen page ER comprises a similar header containing a title PR, a reminder of the patient code CP and the operation date D, and a table listing a series of quantitative tests CT with each of which is associated a "result" field RE which must be completed by the operator, and a "standards" field containing the maximum and minimum values constituting the standards. An icon BA allows the operator to return to the previous screen pages.

A retrospective analysis screen page EA (Fig. 9) must be completed by the operator once the treated cells have been reinjected. This screen page EA contains a header including a stage title RA, the patient code CP and the date D, and a table listing, for a set EXA of tests PH, CX, CS, BS carried out after reinjection, the results RE which must be entered by the operator and, opposite each result, the corresponding standard NO.

Final certification of a preparation is obtained from a specific screen page EC (Fig. 10) which, in addition to the identification header containing a title FC, the patient code CP and the date D, comprises a declaration CF of final certification providing significant quantitative and qualitative results RF specific sizes and physiological characteristics CF: number of cells, viability, percentage, sterility. There follows a declaration of final

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certification DC in which there is an indication Yes (Y) or No (N) of whether final certification has in fact been granted to this preparation. An alarm icon AI prompts the operator to consult a screen page EI (Fig. 11) listing the anomalies detected during the process. On the final certification screen page EC, a specific icon PC allows the operator to pass to the screen page ET (Fig.12) for the transfer of the preparation to the treatment centre. Moreover, a print command PR, a validation command VA and a cancellation command CA are normally provided. It is to be noted that this certification screen page EC can only be validated after a password has been entered and checked, for reasons of certification security.

The anomalies screen page EI comprises a header including a title LI, a reminder of the patient code CP, of the date D, of the study ST and of the batch number LN. There follows a list I1-I4 of anomalies detected during the process with an indication of the remedies which have been applied. This screen page EI further comprises an indication NI of the number of anomalies checked and an indication TI of the total number of anomalies. A message IN prompts the operator to consult the screen page corresponding to a given anomaly by double clicking on the required anomaly using the mouse. After optional consultation of this anomalies screen page, the operator can then consulter and process the screen page ET for transfer to the treatment centre. In addition to a header including a title, this screen page comprises a reminder of the patient code CP, of the study ST and of the date D, on the one hand a set of data LAB characteristic of the laboratory responsible for the preparation, and on the other hand the details TC of the treatment centre to which the preparation is destined.

The characteristics LAB include, for the laboratory, the name LA, the postal address AD, the telephone and fax numbers TL, FA, and the name CL of the person in charge of the preparation. The information TC relating to the treatment centre includes its title TR, its address AD, its telephone

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and fax numbers TL, FA and the name PI of the person in charge of this treatment.

A message MA warns the operator that this screen page must be printed, further comprising, for example at the bottom of the page, information relating to transmission and reception operations. In this way, the transmission EN and reception ER lines must be completed by the operator for the following fields: dates DS, DR; times TS, TR and persons in charge PS, PT.

Of course, the invention is not limited to the examples which have just been described and numerous developments can be added to these exemples without exceeding the scope of the invention. In this way, this process can be applied to the control and follow-up of quality in many fields other than that of cell therapy. It can moreover be integrated into laboratory automation processes. The process according to the invention also takes account of current concerns relating to biological vigilance and pharmacological vigilance.

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